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- 3) bringing the non-aberrant receptor into contact with a substance which operates the non-aberrant receptor and does not operate the aberrant receptor,
  - 4) determining the operation activity in (3), and
  - 5) comparing the operation activity in step 2) with that of step 4), wherein a similar activity indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.
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J2

16. (three times amended) A method of screening substances for a substance for treatment of a disease in a mammal caused by an aberrant receptor, which has substantially changed affinity for substances that have a natural affinity for a non-aberrant receptor, comprising:

- 1) bringing the aberrant receptor into contact with a substance,
  - 2) determining the operation activity of said substance on said receptor,
  - 3) bringing the non-aberrant receptor into contact with a substance which operates the non-aberrant receptor and does not operate the aberrant receptor,
  - 4) determining the operation activity in (3),
  - 5) comparing the operation activity in step 2) with that of step 4), wherein a similar activity indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, and
  - 6) selecting a substance that causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, wherein the substance can be used to treat a disease caused by the aberrant receptor.
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J3

17. (three times amended) A method of screening for a drug for restoring normal function to a signal transduction system of a cell having an aberrant receptor of a mammal suffering from a disease caused by the aberrant receptor which affects the signal transduction system of the cell, which comprises:

- 1) bringing the aberrant receptor into contact with a subject substance,
- 2) determining the activity of said substance on said receptor,
- 3) bringing the non-aberrant receptor into contact with a substance which operates a non-aberrant receptor and does not operate the aberrant receptor,
- 4) determining the operation activity in (3),

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5) comparing the operation activity in step 2) with that of step 4), wherein a similar activity indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, and

6) selecting a substance that causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, wherein the activity is an activity that restores the normal function of the cell.

21. (three times amended) A method of preparing a substance for treatment of a disease in a mammal caused by an aberrant receptor having a substantially changed affinity for substances, which results in the substantial reduction in activity of the signal transduction system of cells having the aberrant receptor, the method comprising:

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bringing the aberrant receptor into contact with a subject substance,  
assaying the activity of said substance on the aberrant receptor,  
selecting a substance that substantially operates the signal transduction system of the cell having the aberrant receptor wherein said activity is activity that increases activity of the signal transduction system of the cell,  
and admixing the selected substance with a pharmaceutically acceptable carrier.

24. (four times amended) A method of screening for a substance capable of causing an aberrant receptor, which has substantially changed affinity for substances, to operate in a manner similar to a non-aberrant receptor comprising:

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(1) expressing in a cell the gene encoding the aberrant receptor,  
(2) isolating the aberrant receptor from the cell,  
(3) providing a substance to the aberrant receptor,  
(4) determining the operation activity of the substance on the receptor, and  
(5) bringing the non-aberrant receptor into contact with a substance which operates the non-aberrant receptor and does not operate the aberrant receptor,  
(6) determining the operation activity in (5),

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cont. (7) comparing the operation activity in step 4) with that of step 6), wherein a similar activity indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.

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27. (amended) A method of screening for a substance capable of causing an aberrant receptor, which has substantially changed affinity for substances that have a natural affinity for a non-aberrant receptor, to operate in a manner similar to a non-aberrant receptor comprising:

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- (1) providing cells expressing the gene encoding the aberrant receptor,
  - (2) providing the substance to be screened to the cells expressing the aberrant receptor,
  - (3) determining the operation activity of said substance on said receptor,
  - (4) providing cells expressing the gene encoding the non-aberrant receptor,
  - (5) providing to the cells expressing the non-aberrant receptor a substance which operates the non-aberrant receptor and not operate the aberrant receptor,
  - (6) determining the operation activity in (5), and
  - (7) comparing the operation activity in step (3) with that of step (6), wherein a similar activity indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.
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Please add the following new claims:

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-- 39. A method of screening subject substances for a substance capable of causing an aberrant receptor, which has substantially changed affinity for natural substances that have a natural affinity for a non-aberrant receptor, to operate in a manner similar to the non-aberrant receptor comprising:

- 1) bringing the aberrant receptor into contact with a subject substance, said subject substance comprising a synthetic compound which substantially fails to operate the non-aberrant receptor,
- 2) determining the operation activity of said subject substance on said receptor,

- 3) bringing the non-aberrant receptor into contact with a natural substance which operates the non-aberrant receptor and does not operate the aberrant receptor,
- 4) determining the operation activity in (3), and
- 5) comparing the operation activity in step (2) with that of step (4), wherein a similar activity indicates that the subject substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.

40. A method of screening subject substances for use in treatment of a disease in a mammal caused by an aberrant receptor, which has substantially changed affinity for natural substances that have a natural affinity for a non-aberrant receptor, comprising:

- 1) bringing the aberrant receptor into contact with a subject substance, said subject substance comprising a synthetic compound which substantially fails to operate the non-aberrant receptor,
- 2) determining the operation activity of said subject substance on said receptor,
- 3) bringing the non-aberrant receptor into contact with a natural substance which operates the non-aberrant receptor and does not operate the aberrant receptor,
- 4) determining the operation activity in (3),
- 5) comparing the operation activity in step 2) with that of step 4), wherein a similar activity indicates that the subject substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, and
- 6) selecting a subject substance that causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, wherein the substance can be used to treat a disease caused by the aberrant receptor.

41. A method of screening for a drug for restoring normal function to a signal transduction system of a cell having an aberrant receptor of a mammal suffering from a disease caused by the aberrant receptor which affects the signal transduction system of the cell, which comprises:

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- 1) bringing the aberrant receptor into contact with a subject substance, said subject substance comprising a synthetic compound which substantially fails to operate the non-aberrant receptor,
- 2) determining the activity of said subject substance on said receptor,
- 3) bringing the non-aberrant receptor into contact with a natural substance which operates a non-aberrant receptor and does not operate the aberrant receptor,
- 4) determining the operation activity in (3),
- 5) comparing the operation activity in step 2) with that of step 4), wherein a similar activity indicates that the subject substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, and
- 6) selecting a subject substance that causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, wherein the activity is an activity that restores the normal function of the cell.

42. A method of preparing a substance for treatment of a disease in a mammal caused by an aberrant receptor having a substantially changed affinity for natural substances, which results in the substantial reduction in activity of the signal transduction system of cells having the aberrant receptor, the method comprising:

bringing the aberrant receptor into contact with a subject substance, said subject substance comprising a synthetic compound which substantially fails to operate the non-aberrant receptor,

assaying the activity of said subject substance on the aberrant receptor,

selecting a subject substance that substantially operates the signal transduction system of the cell having the aberrant receptor wherein said activity is activity that increases activity of the signal transduction system of the cell,

and admixing the selected substance with a pharmaceutically acceptable carrier.

43. A method of screening for a substance capable of causing an aberrant receptor, which has substantially changed affinity for natural substances, to operate in a manner similar to a non-aberrant receptor comprising:

- (1) expressing in a cell the gene encoding the aberrant receptor,

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- (2) isolating the aberrant receptor from the cell,
- (3) providing a subject substance to the aberrant receptor, said subject substance comprising a synthetic compound which substantially fails to operate the non-aberrant receptor,
- (4) determining the operation activity of the subject substance on the receptor, and
- (5) bringing the non-aberrant receptor into contact with a natural substance which operates the non-aberrant receptor and does not operate the aberrant receptor,
- (6) determining the operation activity in (5),
- (7) comparing the operation activity in step 4) with that of step 6), wherein a similar activity indicates that the subject substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.

44. A method of screening for a substance capable of causing an aberrant receptor, which has substantially changed affinity for natural substances that have a natural affinity for a non-aberrant receptor, to operate in a manner similar to a non-aberrant receptor comprising:

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- (1) providing cells expressing the gene encoding the aberrant receptor,
  - (2) providing ~~the~~ a subject substance to be screened to the cells expressing the aberrant receptor, said subject substance comprising a synthetic compound which substantially fails to operate the non-aberrant receptor,
  - (3) determining the operation activity of said subject substance on said receptor,
  - (4) providing cells expressing the gene encoding the non-aberrant receptor,
  - (5) providing to the cells expressing the non-aberrant receptor a natural substance which operates the non-aberrant receptor and not operate the aberrant receptor,
  - (6) determining the operation activity in (5), and
  - (7) comparing the operation activity in step (3) with that of step (6), wherein a similar activity indicates that the subject substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor. --
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*cont.*